

REMARKS

Objection to the Specification and Rejection of Claims 16-17 Under 35 U.S.C. § 112, First Paragraph:

The Examiner has maintained the objection to the specification and rejection of Claims 16-17 under 35 U.S.C. § 112, first paragraph, on the basis of enablement.

To expedite prosecution, Applicants have cancelled Claims 16-17, without prejudice to or disclaimer of the subject matter therein. Applicants expressly reserve the right to pursue the subject matter of these claims in a continuation application.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of Claims 16-17 under 35 U.S.C. § 112, first paragraph.

Rejection of Claims 1-3, 9 and 14-15 Under 35 U.S.C. § 103:

The Examiner has maintained the rejection of Claims 1-3, 9 and 14-15 under 35 U.S.C. § 103, contending that these claims are not patentable over Zhang et al. in view of Lenardo. In response to Applicants' last reply, the Examiner asserted that Applicants failed to consider the combination of references in light of what would be known by the artisan of ordinary skill. Specifically, the Examiner contends that if Zhang et al. teach a method to stimulate memory T cells, and Lenardo teach a method to protect mature T activated cells (a stage through which memory T cells most likely pass, according to the Examiner), then it is allegedly obvious to provide an adjuvant (for stimulating any aspect of the T cell response) comprising an agent that increases T cell activity and one that decreases T cell activity. The Examiner further states that the specification provides essentially no data and discloses merely the concept of the claimed adjuvant, in reply to Applicants' arguments regarding expectation of success provided by the combination of references.

Applicants traverse the Examiner's rejection of Claims 1-3, 9 and 14-15 under 35 U.S.C. § 103. Initially Applicants submit that the combination of references were not viewed in a vacuum, but were indeed viewed in light of what would have been known at the time of the invention by one of ordinary skill in the art. In the remarks on page 4 of the October 18 Office Action, the Examiner distills the teachings of the combination of references to two most general teachings of (a) a method to stimulate memory T cells (Zhang et al.) and (b) a method to protect mature activated T cells, some

of which may ultimately become memory T cells (Lenardo). However, Applicants submit that one of skill in the art, in considering the references, would in fact evaluate the actual details of the references, and in doing so, would simply not arrive at the present invention, particularly in view of these teachings and the knowledge in the art at the time of the invention. To infer some other specific motivations or teachings that are not present in the combination of references or to avoid reading all of the teachings of the references when evaluating the combination does not fairly consider the references as a whole or the desirability of making the combination. (See MPEP 2141.02: "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. vs. Garlock, Inc.* 721 F.2d 1540, 220 USPQ 303, (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)"). Applicants submit that in the Amendment and Response filed July 27, 2004, portions of Zhang et al. that, alone or in combination with Lenardo, *teach away* from the present invention, were not specifically addressed by the Examiner. In this response, Applicants will try to clarify the argument and present further evidence that Lenardo also effectively *teaches away* from the claimed invention.

With regard to Zhang et al., the Examiner states that this reference teaches a method to stimulate memory T cells. However, as Applicants have previously argued, one of skill in the art will more specifically learn from the teachings of Zhang et al. that while IL-15 stimulates T cells that are restricted to a memory phenotype, Zhang et al. also teach that IL-2 caused minimal or insignificant *stimulation* of CD4⁺ and CD8⁺ T cells that was restricted to memory-phenotype cells, and do not teach or suggest that IL-2 should be inhibited. Therefore, the only teaching or motivation to provide an agent that blocks IL-2 in the claimed vaccine adjuvant would have to come from Lenardo according to the Examiner's combination. However, Applicants submit that even viewing Lenardo and the combination of references as a whole, one of skill in the art would not discount the fact that Zhang et al. teach that IL-2 can mildly *stimulate* T cells of a memory phenotype. Applicants submit that minimally, one of skill in the art viewing the teachings of Zhang et al. would do nothing with regard to IL-2, or would *provide* IL-2 to try to achieve at least the minimal added stimulation of memory phenotype observed by Zhang et al. According to the teachings of Zhang et al., for one of skill in the art to combine IL-15 with an agent that inhibits IL-2 would be either pointless or actually conflict with the goal of adding the IL-15.

Furthermore, Applicants submit that the combination of Zhang et al. with Lenardo does not overcome or modify the teachings of Zhang et al. with regard to IL-2. First, as previously set forth by Applicants, Lenardo is not directed to T cells of a memory phenotype at all. Second, a careful reading of Lenardo also reveals a *teaching away* from the present invention. On the first point, the Examiner refers to the teachings of Lenardo and submits that one of skill in the art would select to provide an agent that decreases IL-2 activity, apparently on the basis that Lenardo teaches a method to protect mature activated T cells, which the Examiner argues is a stage through which memory T cells likely pass. However, Applicants submit that one of skill in the art viewing Lenardo would not provide an agent that decreases IL-2 activity in an adjuvant that is otherwise directed to stimulating memory T cells, because Lenardo only evaluates the effects of the administration of *antigen and* IL-2 (or *antigen and* the 3C7 antibody that blocks IL-2 activity by blocking the IL-2 receptor) on activation of mature T cells. Indeed, Lenardo do not know or evaluate the effect of IL-2 on memory T cells but merely speculate that memory T cells might escape death induced by antigen stimulation and IL-2 (see page 861). Therefore, at best, one of skill in the art reviewing this section might speculate from the teachings of Lenardo that IL-2 has either no effect on the development of T cells of a memory phenotype, or might stimulate their development or survival, but would have no basis to conclude that inhibition of IL-2 would cause stimulation of T cells of a memory phenotype.

On the second point, even if one of skill in the art viewed Lenardo as a teaching that one should protect mature activated T cells in order to increase the development/survival of memory T cells, Applicants submit that Lenardo *teach away* from inhibiting IL-2 in the absence of concurrently providing an immunizing antigen. Specifically, Lenardo teach that in the absence of antigen stimulation, inhibition of IL-2 (via the 3C7 antibody) has *no effect* on the stimulation of T cells (see page 859, col. 2, first paragraph: "Injection of 3C7 or 11B11 antibody alone had no effect"). Therefore, Lenardo teaches that the use of an agent that inhibits IL-2 in the absence of concurrent antigen stimulation would not be useful for stimulating T cells, in addition to the fact that Lenardo provides no teaching of the effects of any of the treatments on the stimulation of memory T cells. Therefore, the combination of Lenardo with Zhang et al. does not lead one of skill in the art to the claimed invention and in fact, provides a teaching away from the claimed invention.

The Examiner may be implying that one of skill in the art might produce a "composition for stimulating any aspect of the immune response" that includes IL-15 because it stimulates memory T cells and includes an agent that inhibits IL-2 because it protects mature activated T cells. If so, then Applicants submit that the Examiner has not pointed to any motivation in the references themselves to make the combination as the Examiner has done, and further submit that there is no motivation in the art or in the references to combine these teachings. Even if one tried to combine the teachings of Zhang et al. and Lenardo based on a desire to create a new adjuvant, Applicants submit that one of skill in the art would, for the reasons discussed above, arrive at the conclusion that using an agent that inhibits IL-2 in combination with IL-15 would be either detrimental or not useful for the goal of producing T cells of a memory phenotype. Similarly, Zhang et al. teach that IL-15 is largely selective for the stimulation of T cells of a memory phenotype (see Summary), and so one finds no motivation in Zhang et al. or in Lenardo (which is directed to activation of mature T cells) to combine IL-15 with an IL-2 inhibitor, as one of skill in the art is provided with no expected benefit for the activation of mature T cells by the presence of IL-15. Finally, in the absence of providing antigen, one would not even expect a benefit on mature T cells from the inclusion of an IL-2 inhibitor, given the cited teachings. Therefore, one of skill in the art would not make the combination of agents in view of the teachings of Zhang et al. and Lenardo.

The combination of references cited by the Examiner must not only teach the elements of an agent that stimulates IL-15 and an agent that inhibits IL-2, but also provide some basis for providing an adjuvant that contains both components. Applicants submit that, for the reasons above, one of skill in the art, viewing the combination of references cited by the Examiner, would not find it obvious at all to combine such agents to produce the claimed adjuvant. In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-3, 9 and 14-15 under 35 U.S.C. § 103.

Applicants have attempted to respond to all of the Examiner's concerns as set forth in the October 18 Office Action and submit that the claims are in a condition for allowance. In the event that the Examiner has additional questions regarding Applicants' position, he is respectfully encouraged to contact the below-named agent at (303) 863-9700 to expedite prosecution of the claims.

Respectfully submitted,

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